



SEQUENCE LISTING

<110> Roy A. Gravel et al.

<120> HUMAN METHIONINE SYNTHASE REDUCTASE:
CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE
DEFECTS, CARDIOVASCULAR DISEASE, AND CANCER

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<141> 1999-08-10

<150> 60/071,622

<151> 1998-01-16

<150> 09/232,028

<151> 1999-01-15

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Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr
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Thr Asp Leu Val Lys Ser Glu Leu Leu His Ile Glu Ser Gln Val Glu
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Leu	Arg	His	Phe	Leu	Lys	His	Gly	Ile	Leu	Thr	His	Leu	Lys	Val	Ser
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 Ala Lys Asp Val His Asp Ala Leu Val Gln Ile Ile Ser Lys Glu Val
 660 665 670
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 Lys Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His
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 305 310 315 320
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Ser Cys Gln Pro Pro Leu Ser Leu Leu Leu Glu His Leu Pro Lys Leu				
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Gln Pro Arg Pro Tyr Ser Cys Ala Ser Ser Ser Leu Phe His Pro Gly				
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Phe Ser Arg Asp Ala Pro Val Gly Glu Glu Glu Ala Pro Ala Lys Tyr				
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Val Gln Asp Asn Ile Gln Leu His Gly Gln Gln Val Ala Arg Ile Leu				
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Leu Gln Glu Asn Gly His Ile Tyr Val Cys Gly Asp Ala Lys Asn Met				
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Ala Pro Asp Asn Cys Ala Arg Phe Val Arg Arg Ile Asn Arg Asn Ser			
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Leu Glu Asn Glu Tyr Leu Lys Asn Leu Asp Tyr Val Leu Leu Gly Leu			
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Gly Asp Ser Asn Tyr Ser Ser Tyr Gln Thr Ile Pro Arg Lys Ile Asp			
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Lys Gln Leu Thr Ala Leu Gly Ala Asn Arg Leu Phe Asp Arg Ala Glu			
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Ala Asp Asp Gln Val Gly Leu Glu Leu Glu Val Glu Pro Trp Ile Glu			
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Lys Phe Phe Ala Thr Leu Ala Ser Arg Phe Asp Ile Ser Ala Asp Lys			
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Thr Glu Glu Glu Lys Lys Ala Leu Leu Gln Lys Arg Ile Glu Asp Glu			
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Glu Ser Asp Asp Glu Gly Arg Gly Arg Val Ile Gly Ile Asp Met Leu			
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Ile Pro Glu His Tyr Asp Tyr Pro Glu Ile Ser Leu Leu Lys Gly Ser			
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Gln Thr Leu Ser Asn Asp Glu Asn Leu Arg Val Pro Ile Ala Pro Gln			
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Pro Phe Ile Val Ser Ser Val Ser Asn Arg Lys Leu Pro Glu Asp Thr			
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Lys Leu Glu Trp Gln Asn Leu Cys Lys Met Pro Gly Val Val Thr Lys			
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Pro Phe Glu Val Leu Val Val Ser Ala Glu Phe Val Thr Asp Pro Phe			
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Val Leu Asp Ile Ala Asp Gln Gln Cys Glu Leu Ser Ile Asn Pro Lys			
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Glu Lys Arg Arg Leu Leu Glu Leu Cys Ser Ala Gln Gly Met Lys Asp			
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Arg Lys Ala Arg Leu Ile Tyr Ser Glu Met Glu Phe Pro Ala Thr Asp
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Gly Arg Arg His Ser Arg Lys Gly Leu Ala Thr Asp Trp Leu Asn Ser
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Pro Leu Leu Met Val Gly Pro Gly Thr Gly Val Ser Val Phe Leu Ser
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Gln Asp Gly Leu Arg Lys Tyr Leu Asp Lys Val Leu Pro Phe Leu Thr
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Ala Ser Thr Glu Ser Lys Ile Phe Ile Cys Gly Asp Ala Lys Gly Met
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50 55 60
Arg Glu Ser Ser Phe Val Glu Lys Met Lys Lys Thr Gly Arg Asn Ile
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Thr	Tyr	Glu	His	Phe	Asn	Ala	Met	Gly	Lys	Tyr	Val	Asp	Lys	Arg	Leu
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 <212> PRT
 <213> Homo sapiens

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 35 40 45
 Glu Thr Ala Pro Leu Val Val Val Ser Thr Thr Gly Thr Gly Asp
 50 55 60
 Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr
 65 70 75 80
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Lys	Arg	Leu	Gln	Glu	Leu	Gly	Ala	Arg	His	Phe	Tyr	Asp	Thr	Gly	His				
			115				120						125						
Ala	Asp	Asp	Cys	Val	Gly	Leu	Glu	Leu	Val	Val	Glu	Pro	Trp	Ile	Ala				
			130				135						140						
Gly	Leu	Trp	Pro	Ala	Leu	Arg	Lys	His	Phe	Arg	Ser	Ser	Arg	Gly	Gln				
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Glu	Glu	Ile	Ser	Gly	Ala	Leu	Pro	Val	Ala	Ser	Pro	Ala	Ser	Leu	Arg				
			165				170						175						
Thr	Asp	Leu	Val	Lys	Ser	Glu	Leu	Leu	His	Ile	Glu	Ser	Gln	Val	Glu				
			180				185						190						
Leu	Leu	Arg	Phe	Asp	Asp	Ser	Gly	Arg	Lys	Asp	Ser	Glu	Val	Leu	Lys				
			195				200						205						
Gln	Asn	Ala	Val	Asn	Ser	Asn	Gln	Ser	Asn	Val	Val	Ile	Glu	Asp	Phe				
			210				215						220						
Glu	Ser	Ser	Leu	Thr	Arg	Ser	Val	Pro	Pro	Leu	Ser	Gln	Ala	Ser	Leu				
225							230						235						
Asn	Ile	Pro	Gly	Leu	Pro	Pro	Glu	Tyr	Leu	Gln	Val	His	Leu	Gln	Glu				
			245				250						255						
Ser	Leu	Gly	Gln	Glu	Glu	Ser	Gln	Val	Ser	Val	Thr	Ser	Ala	Asp	Pro				
			260				265						270						
Val	Phe	Gln	Val	Pro	Ile	Ser	Lys	Ala	Val	Gln	Leu	Thr	Thr	Asn	Asp				
			275				280						285						
Ala	Ile	Lys	Thr	Thr	Leu	Leu	Val	Glu	Leu	Asp	Ile	Ser	Asn	Thr	Asp				
			290				295						300						
Phe	Ser	Tyr	Gln	Pro	Gly	Asp	Ala	Phe	Ser	Val	Ile	Cys	Pro	Asn	Ser				
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Asp	Ser	Glu	Val	Gln	Ser	Leu	Leu	Gln	Arg	Leu	Gln	Leu	Glu	Asp	Lys				
			325				330						335						
Arg	Glu	His	Cys	Val	Leu	Leu	Lys	Ile	Lys	Ala	Asp	Thr	Lys	Lys	Lys				
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Gly	Ala	Thr	Leu	Pro	Gln	His	Ile	Pro	Ala	Gly	Cys	Ser	Leu	Gln	Phe				
			355				360						365						
Ile	Phe	Thr	Trp	Cys	Leu	Glu	Ile	Arg	Ala	Ile	Pro	Lys	Lys	Ala	Phe				
			370				375						380						
Leu	Arg	Ala	Leu	Val	Asp	Tyr	Thr	Ser	Asp	Ser	Ala	Glu	Lys	Arg	Arg				
385							390						395						
Leu	Gln	Glu	Leu	Cys	Ser	Lys	Gln	Gly	Ala	Ala	Asp	Tyr	Ser	Arg	Phe				
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Val	Arg	Asp	Ala	Cys	Ala	Cys	Leu	Leu	Asp	Leu	Leu	Leu	Ala	Phe	Pro				
			420				425						430						
Ser	Cys	Gln	Pro	Pro	Leu	Ser	Leu	Leu	Glu	His	Leu	Pro	Lys	Leu					
			435				440						445						
Gln	Pro	Arg	Pro	Tyr	Ser	Cys	Ala	Ser	Ser	Ser	Leu	Phe	His	Pro	Gly				
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Thr	Glu	Val	Leu	Arg	Lys	Gly	Val	Cys	Thr	Gly	Trp	Leu	Ala	Leu	Leu				
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Val	Ala	Ser	Val	Leu	Gln	Pro	Asn	Ile	His	Ala	Ser	His	Glu	Asp	Ser
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Gly	Lys	Ala	Leu	Ala	Pro	Lys	Ile	Ser	Ile	Ser	Pro	Arg	Thr	Thr	Asn
		515					520					525			
Ser	Phe	His	Leu	Pro	Asp	Asp	Pro	Ser	Ile	Pro	Ile	Ile	Met	Val	Gly
	530					535					540				
Pro	Gly	Thr	Gly	Ile	Ala	Pro	Phe	Ile	Gly	Phe	Leu	Gln	His	Arg	Glu
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Lys	Leu	Gln	Glu	Gln	His	Pro	Asp	Gly	Asn	Phe	Gly	Ala	Met	Trp	Leu
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Phe	Phe	Gly	Cys	Arg	His	Lys	Asp	Arg	Asp	Tyr	Leu	Phe	Arg	Lys	Glu
			580					585					590		
Leu	Arg	His	Phe	Leu	Lys	His	Gly	Ile	Leu	Thr	His	Leu	Lys	Val	Ser
		595					600					605			
Phe	Ser	Arg	Asp	Ala	Pro	Val	Gly	Glu	Glu	Glu	Ala	Pro	Ala	Lys	Tyr
	610					615					620				
Val	Gln	Asp	Asn	Ile	Gln	Leu	His	Gly	Gln	Gln	Val	Ala	Arg	Ile	Leu
625					630					635					640
Leu	Gln	Glu	Asn	Gly	His	Ile	Tyr	Val	Cys	Gly	Asp	Ala	Lys	Asn	Met
				645					650					655	
Ala	Lys	Asp	Val	His	Asp	Ala	Leu	Val	Gln	Ile	Ile	Ser	Lys	Glu	Val
			660					665					670		
Gly	Val	Glu	Lys	Leu	Glu	Ala	Met	Lys	Thr	Leu	Ala	Thr	Leu	Lys	Glu
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 <212> DNA
 <213> Homo sapiens

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tacacctact tttgcaatgg ggggaagata attgataaac gacttcaaga gcttgagacc	360
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gtccttttga aaataaaggc agacacaaaag aagaaaggag ctaccttacc ccagcatata	1080

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gatgcccttg tgcaaataat aagcaaagag gttggagttg aaaaactaga agcaatgaaa 2040
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<210> 46
 <211> 697
 <212> PRT
 <213> Homo sapiens

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Ala Asp Leu His Cys Ile Ser Glu Ser Asp Lys Tyr Asp Leu Lys Thr
 35          40          45
Glu Thr Ala Pro Leu Val Val Val Ser Thr Thr Gly Thr Gly Asp
 50          55          60
Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr
 65          70          75          80
Leu Pro Val Asp Phe Phe Ala His Leu Arg Tyr Gly Leu Leu Gly Leu
 85          90          95
Gly Asp Ser Glu Tyr Thr Tyr Phe Cys Asn Gly Gly Lys Ile Ile Asp
100         105         110
Lys Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His
115         120         125
Ala Asp Asp Cys Val Gly Leu Glu Leu Val Val Glu Pro Trp Ile Ala
130         135         140
Gly Leu Trp Pro Ala Leu Arg Lys His Phe Arg Ser Ser Arg Gly Gln
145         150         155         160
Glu Glu Ile Ser Gly Ala Leu Pro Val Ala Ser Pro Ala Ser Leu Arg
165         170         175
Thr Asp Leu Val Lys Ser Glu Leu Leu His Ile Glu Ser Gln Val Glu
180         185         190
Leu Leu Arg Phe Asp Asp Ser Gly Arg Lys Asp Ser Glu Val Leu Lys
195         200         205
Gln Asn Ala Val Asn Ser Asn Gln Ser Asn Val Val Ile Glu Asp Phe

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210		215		220
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Asn Ile Pro Gly Leu Pro	Pro Glu Tyr Leu Gln Val His Leu Gln Glu			
245	250	255		
Ser Leu Gly Gln Glu Glu	Ser Gln Val Ser Val Thr Ser Ala Asp Pro			
260	265	270		
Val Phe Gln Val Pro Ile	Ser Lys Ala Val Gln Leu Thr Thr Asn Asp			
275	280	285		
Ala Ile Lys Thr Thr Leu	Leu Val Glu Leu Asp Ile Ser Asn Thr Asp			
290	295	300		
Phe Ser Tyr Gln Pro Gly	Asp Ala Phe Ser Val Ile Cys Pro Asn Ser			
305	310	315	320	
Asp Ser Glu Val Gln Ser	Leu Leu Gln Arg Leu Gln Leu Glu Asp Lys			
325	330	335		
Arg Glu His Cys Val Leu	Leu Lys Ile Lys Ala Asp Thr Lys Lys Lys			
340	345	350		
Gly Ala Thr Leu Pro Gln	His Ile Pro Ala Gly Cys Ser Leu Gln Phe			
355	360	365		
Ile Phe Thr Trp Cys Leu	Glu Ile Arg Ala Ile Pro Lys Lys Ala Phe			
370	375	380		
Leu Arg Ala Leu Val Asp	Tyr Thr Ser Asp Ser Ala Glu Lys Arg Arg			
385	390	395	400	
Leu Gln Glu Leu Cys Ser	Lys Gln Gly Ala Ala Asp Tyr Ser Arg Phe			
405	410	415		
Val Arg Asp Ala Cys Ala	Cys Leu Leu Asp Leu Leu Leu Ala Phe Pro			
420	425	430		
Ser Cys Gln Pro Pro Leu	Ser Leu Leu Leu Glu His Leu Pro Lys Leu			
435	440	445		
Gln Pro Arg Pro Tyr Ser	Cys Ala Ser Ser Ser Leu Phe His Pro Gly			
450	455	460		
Lys Leu His Phe Val Phe	Asn Ile Val Glu Phe Leu Ser Thr Ala Thr			
465	470	475	480	
Thr Glu Val Leu Arg Lys	Gly Val Cys Thr Gly Trp Leu Ala Leu Leu			
485	490	495		
Val Ala Ser Val Leu Gln	Pro Asn Ile His Ala Ser His Glu Asp Ser			
500	505	510		
Gly Lys Ala Leu Ala Pro	Lys Ile Ser Ile Ser Pro Arg Thr Thr Asn			
515	520	525		
Ser Phe His Leu Pro Asp	Asp Pro Ser Ile Pro Ile Ile Met Val Gly			
530	535	540		
Pro Gly Thr Gly Ile Ala	Pro Phe Ile Gly Phe Leu Gln His Arg Glu			
545	550	555	560	
Lys Leu Gln Glu Gln His	Pro Asp Gly Asn Phe Gly Ala Met Trp Phe			
565	570	575		
Phe Gly Cys Arg His Lys	Asp Arg Asp Tyr Leu Phe Arg Lys Glu Leu			
580	585	590		
Arg His Phe Leu Lys His	Gly Ile Leu Thr His Leu Lys Val Ser Phe			
595	600	605		
Ser Arg Asp Ala Pro Val	Gly Glu Glu Glu Ala Pro Ala Lys Tyr Val			
610	615	620		

Gln Asp Asn Ile Gln Leu His Gly Gln Gln Val Ala Arg Ile Leu Leu
 625 630 635 640
 Gln Glu Asn Gly His Ile Tyr Val Cys Gly Asp Ala Lys Asn Met Ala
 645 650 655
 Lys Asp Val His Asp Ala Leu Val Gln Ile Ile Ser Lys Glu Val Gly
 660 665 670
 Val Glu Lys Leu Glu Ala Met Lys Thr Leu Ala Thr Leu Lys Glu Glu
 675 680 685
 Lys Arg Tyr Leu Gln Asp Ile Trp Ser
 690 695

<210> 47
 <211> 2093
 <212> DNA
 <213> Homo sapiens

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2093

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 <211> 689
 <212> PRT
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 35 40 45
 Thr Ala Pro Leu Val Val Val Val Ser Thr Thr Gly Thr Gly Asp Pro
 50 55 60
 Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr Leu
 65 70 75 80
 Pro Val Asp Phe Phe Ala His Leu Arg Tyr Gly Leu Leu Gly Leu Gly
 85 90 95
 Asp Ser Glu Tyr Thr Tyr Phe Cys Asn Gly Gly Lys Ile Ile Asp Lys
 100 105 110
 Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His Ala
 115 120 125
 Asp Asp Cys Val Gly Leu Glu Leu Val Val Glu Pro Trp Ile Ala Gly
 130 135 140
 Leu Trp Pro Ala Leu Arg Lys His Phe Arg Ser Ser Arg Gly Gln Glu
 145 150 155 160
 Glu Ile Ser Gly Ala Leu Pro Val Ala Ser Pro Ala Ser Leu Arg Thr
 165 170 175
 Asp Leu Val Lys Ser Glu Leu Leu His Ile Glu Ser Gln Val Glu Leu
 180 185 190
 Leu Arg Phe Asp Asp Ser Gly Arg Lys Asp Ser Glu Val Leu Lys Gln
 195 200 205
 Asn Ala Val Asn Ser Asn Gln Ser Asn Val Val Ile Glu Asp Phe Glu
 210 215 220
 Ser Ser Leu Thr Arg Ser Val Pro Pro Leu Ser Gln Ala Ser Leu Asn
 225 230 235 240
 Ile Pro Gly Leu Pro Pro Glu Tyr Leu Gln Val His Leu Gln Glu Ser
 245 250 255
 Leu Gly Gln Glu Glu Ser Gln Val Ser Val Thr Ser Ala Asp Pro Val
 260 265 270
 Phe Gln Val Pro Ile Ser Lys Ala Val Gln Leu Thr Thr Asn Asp Ala
 275 280 285
 Ile Lys Thr Thr Leu Leu Val Glu Leu Asp Ile Ser Asn Thr Asp Phe
 290 295 300
 Ser Tyr Gln Pro Gly Asp Ala Phe Ser Val Ile Cys Pro Asn Ser Asp
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<210> 50
<211> 26
<212> DNA
<213> Homo sapiens

<400> 50
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<210> 51
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